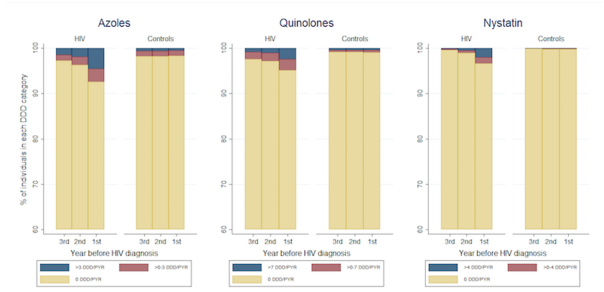

Figure 2b

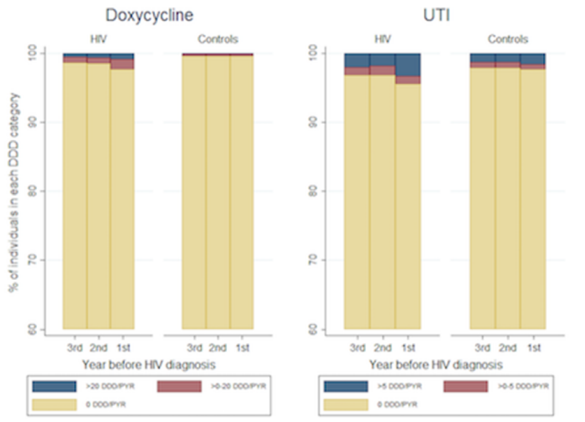

Figure 2c

DDD/3PYR	HIV (%)	Controls (%)	OR (95% CI)
Beta-lactams			
>0 vs 0	1533 (55·1)	13315 (36·8)	2·13 (1·97·2·30)
>10 vs ≤ 10	1032 (37·1)	7485 (20·7)	2·28 (2·11·2·48)
>20 vs ≤ 20	557 (20·0)	3104 (8·6)	2·70 (2·44·2·98)
>30 vs ≤ 30	333 (12·0)	1508 (4·2)	3·17 (2·79·3·60)
Macrolides			
>0 (vs 0)	932 (33·5)	5037 (13·9)	3·12 (2·87·3·40)
>10 (vs ≤10)	373 (13·4)	1494 (4·1)	3·62 (3·20·4·08)
> 20 (vs ≤20)	170 (6·1)	551 (1·5)	4·26 (3·56·5·08)
Acyclovir			
>0 (vs 0)	353 (12·7)	736 (2·0)	7·20 (6·29·8·25)
>2 (vs ≤2)	279 (10·0)	525 (1·4)	7·78 (6·67·9·08)
>4 (vs ≤ 4)	255 (9·2)	444 (1·2)	8·27 (7·03·9·72)
Azoles			
>0 (vs 0)	310 (11·1)	1448 (4·0)	3·25 (2·84·3·72)
>3 (vs ≤3)	190 (6·8)	574 (1·6)	4·65 (3·92·5·52)
>6 (vs ≤ 6)	160 (5·8)	440 (1·2)	5·01 (4·16·6·04)
Quinolones			
>0 (vs 0)	252 (9·1)	869 (2·4)	4·14 (3·52·4·81)
>7 (vs ≤7)	110 (4·0)	403 (1·1)	3·72 (3·00·4·63)
>14 (vs ≤14)	38 (1·4)	106 (0·3)	4·79 (3·29·6·97)
Nystatin			
>0 (vs 0)	122 (4·4)	164 (0·5)	10·55 (8·27·13·46)
>4 (vs ≤4)	67 (2·4)	72 (0·2)	12·53 (8·94·17·57)
>8 (vs ≤8)	33 (1·2)	25 (0·1)	17·16 (10·21·28·85)
Doxycycline			
>0 (vs 0)	132 (4·7)	386 (1·1)	4·61 (3·77·5·65)
>20 (vs ≤20)	56 (2·0)	95 (0·3)	7·87 (5·63·10·99)
>40 (vs ≤40)	28 (1·0)	45 (0·1)	8·09 (5·05·12·97)
UTI			
>0 (vs 0)	230 (8·3)	1834 (5·1)	1·80 (1·54·2·09)
> 5 (vs ≤5)	165 (5·9)	1190 (3·3)	1·95 (1·64·2·33)
>10 (vs ≤10)	94 (3·4)	635 (1·8)	2·02 (1·61·2·53)

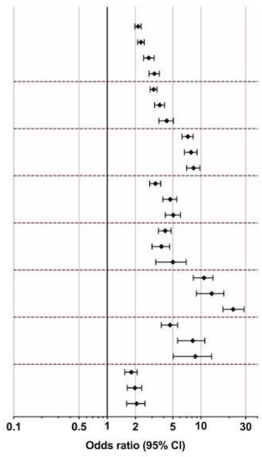

Figure 3. Association between different antimicrobial prescriptions and risk of later HIV infection

BPD3/4

Novel highly potent CD4bs bNAb with restricted pathway to HIV-1 escape

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Purpose: Broadly HIV-1 neutralizing antibodies (bNAbs) can suppress viremia in humans and represent a novel approach for effective immunotherapy. However, bNAb monotherapy selects for antibody-resistant viral variants. Thus, we focused on the identification of new antibody combinations and/or novel bNAbs that restrict pathways of HIV-1 escape.
Methods: We screened HIV-1 positive patients for their neutralizing capacities. Following, we performed single cell sorting and PCR of HIV-1 Env-reactive mature B cells of identified elite neutralizers. Found antibodies were tested for neutralization and binding capacities *in vitro*. Further, their antiviral activity was tested in an HIV-1 infected humanized mouse model.
Results: Here we report the isolation of antibody 1–18, a VH1–46-encoded CD4 binding site (CD4bs) bNAb identified in an individual ranking among the top 1% neutralizers of 2,274 HIV-1-infected subjects. Tested on a 119-virus panel, 1–18 showed to be exceptionally broad and potent with a coverage of 97% and a mean IC50 of 0.048 μg/mL, exceeding the activity of most potent CD4bs bNAbs described to-date. A 2.4 Å cryo-EM structure of 1–18 bound to a native-like Env trimer revealed that it interacts with HIV-1 env similar to other CD4bs bNAbs, but includes additional contacts to the V3 loop of the adjacent protomer. Notably, *in vitro*, 1–18 maintained activity against viruses carrying mutations associated with escape from VRC01-class bNAbs. Further, its HIV-1 env wide escape profile differed critically from other CD4bs bNAbs. In humanized mice, monotherapy with 1–18 was sufficient to prevent the development of viral escape variants that rapidly emerged during treatment with other CD4bs bNAbs. Finally, 1–18 overcame classical HIV-1 mutations that are driven by VRC01-like bNAbs *in vivo*.
Conclusion: 1–18 is a highly potent and broad bNAb that restricts escape and overcomes frequent CD4bs escape pathways, providing new options for bNAb combinations to prevent and treat HIV-1 infection.

BPD3/5

Effect of norethisterone, combined contraceptive vaginal ring (CCVR) and COCPs on HIV cervical target cells in adolescent girls: a randomized crossover study

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Purpose: Majority of new HIV infections in Sub-Saharan Africa occur in adolescent girls and young women, who are also at risk for unintended pregnancies. While a variety of contraceptives are available, the use of progestin-only injectables particularly DMPA, have been associated with increased risk of HIV acquisition. Although the ECHO trial recently revealed that women on DMPA are no more likely to acquire HIV than those using other long-acting methods. We aimed to investigate the effects of NET-EN, combined contraceptive vaginal ring (CCVR) and combined oral contraceptive pills (COCPs) on the frequencies of endocervical T cells, and their expression of CCR5, HLA-DR and CD38.
Method: Adolescent females (n=130; 15–19 years) were randomized 1:1:1 to receive either NET-EN, CCVR, or COCPs, and followed for a total of 32-weeks, crossing over to another HC at 16-weeks. Cervical cytobrush-derived T cells were analyzed by flow cytometry for the expression of CCR5 (HIV co-receptor) and activation markers (HLA-DR and CD38). Paired data was performed using the Wilcoxon signed-rank non-parametric test.
Results: Between baseline and crossover, initiation of CCVR was associated with increased proportions of cervical CD4 + T cells that expressed CD38 singly (p=0.01), and HLA-DR together with CD38 (p=0.03), despite decreased overall frequencies of CD4 + T cells compared to NET-EN and COCPs use. In addition, both CCVR and NET-EN users had increased proportions of CD8 + CD38 + T cells (p=0.01). Interestingly, expression of HLA-DR on CD8 + T cells was reduced at week 16 compared to baseline in all the HC arms.
Conclusion: Although all HC altered the phenotype of cervical CD8 + T cells, the use of the CCVR increased the activation (CD38 +) of both cervical CD4 + and CD8 + T cells in adolescent girls. The use of the CCVR in adolescents at high risk of HIV warrants further investigation.